Registration of FA and T1-Weighted MRI Data of Healthy Human Brain Based on Template Matching and Normalized Cross-Correlation

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Abstract In this work, we propose a new approach for three-dimensional registration of MR fractional anisotropy images with T1-weighted anatomy images of human brain. From the clinical point of view, this accurate coregistration allows precise detection of nerve fibers that is essential in neuroscience. A template matching algorithm combined with normalized cross-correlation was used for this

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registration task. To show the suitability of the proposed method, it was compared with the normalized mutual information-based B-spline registration provided by the Elastix software library, considered a reference method. We also propose a general framework for the evaluation of robustness and reliability of both registration methods. Both registration methods were tested by four evaluation criteria on a dataset consisting of 74 healthy subjects. The template matching algorithm has shown more reliable results than the reference method in registration of the MR fractional anisotropy and T1 anatomy image data. Significant differences were observed in the regions splenium of corpus callosum and genu of corpus callosum, considered very important areas of brain connectivity. We demonstrate that, in this registration task, the currently used mutual informationbased parametric registration can be replaced by more accurate local template matching utilizing the normalized cross-correlation similarity measure.

Keywords Neuroscience · Brain · MRI · Fractional anisotropy · Multimodal image registration · Template matching · Inverse consistency error

Background

Analysis of brain functions and its structure at different scales is a challenging and important issue in neuroscience [1, 2], especially in clinical neuroimaging. Magnetic resonance imaging (MRI) offers acquisitions based on different scan protocols to acquire unique and complementary information about the tissue. Combination of such registered data provides complex information about the structure and function of human brain. The current research deals with accurate and timeefficient multimodal intrasubject MRI registration of high-

	Series	Pulse sequence parameters
1	Localizer 2D	TR/TE=7.8[ms]/1.7[ms]/30[o]; acq. voxel: 1.0×1.0×5.0 [mm3]; 3 [img]
2	Ax PD/T2 2D FSE	TR/TE1/TE2/FA=3840/12.1/84.9/90; voxel: 0.94×0.94×4.0; 52
3	Sag T1 3D FSPGR IR prepped	TR/TE/TI/FA=9.45/2.41/450/7; voxel: 0.94×0.94×1.40; 124
4	Sag T1 3D FSPGR IR prepped	[same as 3 to improve SNR for FreeSurfer segmentation]
5	Ax DTI, EP SE, 26 slices	TR/TE/FA=3840/84.9/90; 25 <i>b</i> =1,000, 5 <i>b</i> =0; voxel: 0.94×0.94×4.0; 780

 Table 1
 MR imaging protocol

resolution T1-weighted images (T1) of anatomy with lowresolution diffusion tensor imaging (DTI) that provides fractional anisotropy (FA) images, containing information about the tissue microarchitecture. Precise spatial alignment of these image data is necessary for applications, especially in the areas such as brain connectivity research [3, 4], preoperative surgical planning [5], and imaging genetics [6, 7]. Precise FA-T1 registration is essential also in the studies of cognitive aging for early recognition of biomarkers describing normal and abnormal degenerations, i.e., Alzheimer [7] and dementia [8].

The DTI is an MRI acquisition technique based on detection of direction and degree of water diffusion in the brain [2, 9]. It allows evaluation of myelinated nerve fibers contributing to anisotropic water diffusion in white matter of the brain and the spinal cord. Further visualization is possible by a fiber tracking technique [10]. In order to describe the position of myelinated nerve fibers within the region of interest in the brain, it is necessary to complement the DTI FA image by additional information about the corresponding anatomical structure of the brain [2, 11]. Then, precise threedimensional (3D) FA-T1 registration is necessary, which allows further reliable statistical evaluation of spatial relations between FA values and anatomy, as needed particularly in case of longitudinal studies of cognitive aging.

Both data sets, T1 and FA, must be preprocessed to suppress acquisition artifacts and to ensure identical geometrical image properties such as resolution and voxel size. Initial spatial alignment of FA and T1 data is usually based on a global rigid or affine geometric transforms [2, 11, 12], followed by a 3D deformable registration method. Li and Verma [13] proposed multimodal feature based image registration using Gabor wavelet transform to create an image collection suitable for multichannel image analysis. Walimuni et al. [14] used the nonlinear image registration tool (FNIRT, http://www.fmrib.ox.ac.uk/fsl/fnirt/) utilizing Gauss–Newton optimization to quantify tissue microstructural integrity. Jahanshad et al. [15] presented a study of brain asymmetry using a fluid registration technique of DTI, T1, and T2 MRI data. Other relevant publications to the problem can be found in [7, 16, 17], as well as in the form of software packages such as ITK [18] and Elastix [19] that are commonly used for image registration.

Although both FA and T1 brain image scans are usually obtained within one MR session, a global affine transform as provided in FMRIB Software Library (FSL, [20]) or FreeSurfer does not ensure precise alignment of local areas in the brain due to geometric distortions, and a nonlinear registration approach is needed. Since the registration of FA and T1 image data is a bimodal registration problem, the normalized mutual information (NMI) seems to be the optimal similarity criterion. However, our approach is based on the verified hypothesis of monotonous intensity dependence between the corresponding two image data sets, which enables using an intensity based similarity. In this paper, we propose a registration approach based on a combination of template matching and the normalized cross-correlation criterion [21]. Computations of correlation via the Fourier

Fig. 1 Preprocessing of DTI FA data (*left* original FA image, *right* segmentation of brain)



Fig. 2 Preprocessing of MRI T1-weighted image data (*left* original, *right* skull strip of brain)



transform domain and parallelization allow a significant reduction of the computational time. The proposed method is compared to the B-spline registration based on NMI, as implemented in the Elastix software (http://elastix.isi.uu.nl), serving here as the reference method. For evaluation of the performance, a general framework based on inverse consistency error (ICE) [22], checkerboard visualization, and nerve fiber intersection (NFI) is suggested and used.

Methods

Image Data Acquisition

The used datasets consist of 3D high-resolution magnetic resonance (MR) T1 weighted images (acquisition matrix, $256 \times 256 \times 124$) and low-resolution DTI-based FA images ($128 \times 128 \times 26$) from 74 elderly people that participated in the longitudinal study "Cognitive Aging" [23, 24]. The project was approved by the Ethical Committee of Western part of Norway. The MR imaging protocol that has been used in this study is described in Table 1. The multimodal MR acquisitions were performed on a 1.5-T GE Signa Echospeed Scanner (MR laboratory, Haraldsplass Deaconess Hospital, Bergen) using a standard eight-channel head coil. The

Fig. 3 Searching for the displacement β_p

participants were instructed to lie still with their eyes closed in the scanner during the MRI examination.

Preprocessing

The DTI data consist of 30 diffusion-weighted (DWI) volumes containing 25 diffusion sensitive (b=1000) directions and 5 baseline (b=0) images without diffusion sensitization. Eddy current distortions of the DWI images caused by local magnetic fields were suppressed by a tool ("Eddy correct") included in the FSL package [18]. The eigen decomposition of the DTI recordings using the Diffusion Toolkit package [25] enabled to estimate the diffusion tensor and determine the voxel-wise FA using the general formula (1)

$$FA = \frac{\sqrt{\left(\lambda_1 - \langle \lambda \rangle\right)^2 + \left(\lambda_2 - \langle \lambda \rangle\right)^2 + \left(\lambda_3 - \langle \lambda \rangle\right)^2}}{\sqrt{2\left(\lambda_1^2 + \lambda_2^2 + \lambda_3^2\right)}}, \qquad (1)$$

where $\langle \lambda \rangle$ determines the mean diffusivity and λ_{1-3} are principal eigenvectors of the diffusion tensor. The skull stripping in FA images (Fig. 1) was performed by the Free-Surfer v.5.0.0, a software library developed at Martinos Center for Biomedical Imaging [26–28].



The anatomical MRI T1-weighted data were geometrically interpolated from their native space $(0.94 \times 0.94 \times$ 1.4 mm) into an isotropic space $(1.0 \times 1.0 \times 1.0 \text{ mm})$ and preprocessed by Freesurfer. The preprocessing included the skull removal (Fig. 2), intensity normalization and labeling of the regions of interest.

Derivation of a Displacement Field via Spectral Domain

The T1 and FA images were registered by the designed template matching (TM) algorithm, which was locally utilized to provide the respective displacement field [8] describing the generic mutual deformation. This algorithm was combined with the normalized cross-correlation criterion to seek the maximum of mutual correlation between the intensity patterns of compared image regions. The main idea of this method is to find the local displacement, which ensures the highest similarity between the template m_p ($k \times l$) extracted from a moving (to be registered) image M, and a corresponding neighborhood f_p ($K \times L$) extracted from a fixed image F. Then, the local displacement β_p is deter-

mined as the difference vector between position A and B that are the central positions of
$$f_p$$
 and the position f_q indicated by the maximum of similarity D (see Fig. 3). The central positions of f_p and m_p should correspond to the same image detail. Searching for the displacement β_p in each node p of a spatial grid (so far regular) is based on the maximization (2) of the normalized cross-correlation criterion D (3),

$$\beta_p = \arg \max_{\beta} D(f_{(p)}, m_{(p+\beta)}), \quad f_p \in F, m_p \in M, \beta_p \in u$$
(2)

where *F* is the fixed image, *M* is the geometrically transformed image, *D* is the similarity measure, β_p denotes the displacement in the node *p* of the defined grid, *u* is the final displacement field, and *p* and *q* are indexes of nodes (spatial positions in the images) and simultaneously the midpoints of *m* and *f* (Fig. 3).The normalized cross correlation used as the similarity criterion for finding the best match of the mask m(i,j) in the neighborhood f(x,y) is defined for two-dimensional case as follows:

$$D(f,m) = \frac{\sum_{i=-k/2}^{k/2} \sum_{j=-l/2}^{l/2} f(x+i,y+j)m(i,j) - kl\mu_f \mu_m}{\left(\left(\sum_{i=-k/2}^{k/2} \sum_{j=-l/2}^{l/2} f^2(x+i,y+j) - kl\mu_f^2\right) \left(\sum_{i=-k/2}^{k/2} \sum_{j=-l/2}^{l/2} m^2(i,j) - kl\mu_m^2\right)\right)^{1/2}},$$
(3)

for all $(x, y) \in K \times L$. Here, μ_f and μ_m denote intensity averages in *m* and *f*. The generalization for the 3D case is straightforward.

The overall computation time is linearly dependent on the number of nodes of the uniformly sampled grid [21]; on the other hand, the grid has to be dense enough to describe the displacement field reliably. The optimal density of the grid, and thus the distribution of its nodes, is set accordingly to the structure of images (Table 2). According to the chosen sampling factor, the displacements can be determined with either pixel or sub-pixel accuracy. The computational demands would be very high when optimizing directly in the original space (3); nevertheless, using the convolution theorem (4)

$$f * m = FFT^{-1} \bigg\{ FFT \{f\} FFT \{m\}^* \bigg\}, \tag{4}$$

Table 2 Parameters ofTM registration	Grid spacing	6×6×6
111 logistititon	Mask	$5 \times 5 \times 5$
	Extent	$11 \times 11 \times 11$

the cross-correlation can be calculated via the Fourier space, where the computational demands are much lower. In this way, the first part of the numerator in Eq. (3) can be rewritten to (disregarding for simplicity the necessary zero padding of the matrices):

$$\sum_{i=-k/2}^{k/2} \sum_{j=-l/2}^{l/2} f(x+i,y+j)m(i,j) = FFT^{-1} \Big(FFT(f)FFT(m)^* \Big).$$
(5)

Impulse-like noise might be present in the resulting displacement field u due to individual falsely found correspondences in homogenous areas without sufficient texture. The displacement

Table 3 Parameters of Elastix registration

Optimizer	Adaptive stochastic gradient descent
Metric	Normalized mutual information
Final grid spacing in physical units	$30 \times 30 \times 30$
Number of resolutions	3
Maximum number of iterations	500

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field u was filtered by peak and valley filter [29] to suppress the impulsive noise and regularized by a Gaussian filter to ensure a global smoothing effect. In order to provide a continuous displacement field for all image points, the displacements were interpolated linearly between the nodes of the used grid. Considering the local optimization and Gaussian filter, we obtain a globally nonlinear regular deformation [25]. Such model can be described as a Gaussian filtered displacement analysis.

Solving the nonparametric registration problem is usually based on using an accurate finite difference scheme [30]; however, the alternative and faster Gaussian filter approximate scheme provides satisfactory results [25, 30, 31]. The convergence of the template matching method is dependent on the deformation extensiveness between images. In case that the deformation is regular enough so that it may be locally considered as shifts, and the search region is large enough, the template matching algorithm [8] in combination with the Gaussian filter [30] turned out to be convergent.

Registration by Elastix

The performance of the proposed registration method was compared with multiresolution B-spline registration with the NMI similarity measure implemented in the free-access Elastix software. The registration parameters were chosen according to the Elastix web database with certain changes suited to the characteristics of FA-T1 data (Table 3). The grid spacing was chosen according to the expected local deformations of structures in the FA images. Different combinations of parameters mentioned in Table 3 were tested in order to achieve the best registration results. The experimentally found optimal setting is mentioned in the second column of this table.

Approaches to the Evaluation of FA-T1 Registration

The evaluation of the presented multimodal registration approach is a demanding and challenging task. Here, an evaluation scheme based on three different methods is considered to provide a good overview on the quality of any FA-T1 registration algorithms. The scheme consists of (1) a formal numerical evaluation of the consistency and robustness called the ICE [22]; (2) a subjective evaluation by checkerboard images, a visual method based on observer's experience; and (3) the Nerve fibers intersection method focused on white matter regions.

Inverse Consistency Error

The ICE criterion (6) evaluates the absolute difference of the regular grid and the grid after composition of the forward and reverse transformations obtained as a result of the forward and reverse registration processes. The forward transformation (FA \rightarrow T1) should be ideally equal to the inverse version of the reverse transformation (T1 \rightarrow FA); a good registration thus should have a minimal ICE value,

Fig. 5 Example of NFI evaluation method (WM segmentation signed by *red line; left* good fit in frontal lobe, *middle* good fit in CSF lobe, *right* fail in genu of corpus callosum part)



Table 4 ICE values from TM and Elastix registrations

	Template matching			Elastix		
	Mean	Max	STD	Mean	Max	STE
Average	1.812	7.022	1.424	2.175	8.173	3.16

$$ICE(\mathbf{x}) = \|\mathbf{t}_{\mathbf{r}}(\mathbf{t}_{\mathbf{f}}(\mathbf{x}) - \mathbf{x})\|.$$
(6)

Here, $\mathbf{t}_{f}(\mathbf{x})$ and $\mathbf{t}_{r}(...)$ are defined as $\mathbf{t}_{f}=\mathbf{x}-\mathbf{u}_{f}$ and $\mathbf{t}_{r}=\mathbf{x}-\mathbf{u}_{r}$, \mathbf{u}_{f} and \mathbf{u}_{r} represent values of the forward and reverse displacement fields, \mathbf{x} is the respective grid position, and || ||denotes the Euclidean norm. The ICE values for each subject were subsequently statistically analyzed by Wilcoxon rank sum test and two-sample *t* test (with parameters df= 146, t_{W} =0.0912, t_{T2} =0.0912, α =0.05). These tests were chosen to show the statistical comparability of the robustness of both registration methods.

Checkerboard Classification Method

Although the evaluation using ICE shows the robustness and reliability of registration algorithms, visual evaluation of results by an expert is necessary for assessment of the practical acceptability. The checkerboard method provides a good overview on the continuity of edges in the checkerboard image compound alternately of registered and target sub-images (Fig. 4). Over thousand slices in six different regions of interest (ROIs) were visually evaluated for both registration methods. These ROIs were specified in the main brain lobes as follows: frontal lobe, parietal lobe, occipital lobe, temporal lobe, cerebrospinal fluid (CSF), and midbrain. The corresponding slices were classified by an expert into five different groups according to the edge continuity: 1, all edges in the region are continuous; 2, most of the edges are continuous; 3, half of the edges are continuous; 4, most of the edges are discontinuous; and 5, no edges are continuous. The scores were provided in each slice independently.

Nerve Fibers Intersection

Table 5Average mean anSTD values marked edge

continuity

As a third criterion, we suggested a new method that evaluates the reliability of fitting the nerve fibers represented by FA values into the white matter (WM) region. The criterion has been implemented in two forms, i.e., as visual evaluation and as automatic assessment; both approaches were compared. This criterion has been used within four regions of interest: frontal, parietal, temporal, and CSF edge.

The visual evaluation utilizes a qualitative classification based comparison of both registration algorithms for each of the above defined WM regions. For this purpose, five classes were defined: 1, all nerve fibers are in the WM region; 2, rare misalignments in the lateral brain regions (about 90 % correctly registered); 3, rare misalignments also in the main brain regions; 4, moderate misalignments in the whole brain; and 5, significant misalignments in the whole brain. This evaluation was performed uniformly for each brain region.

The automatic approach evaluated the intersection of the nerve fibers and the WM region based on the fact that the myelinated nerve fibers are represented by significantly higher intensities in the FA image (Fig. 5). Higher intensity values thus indicate better fitting registration in each of the WM regions. Therefore, the normalized sum of intensity values within each of the WM regions (7) is calculated

$$NFI_{val} = \frac{1}{M} \sum_{i \in \Psi} FA(i), \tag{7}$$

where Ψ is the selected WM region (defined using the Freesurfer), M is the size of a selected region, and i is the index of WM image point.

Implementation and Testing

The registration algorithms were both tested on the same high-performance computational cluster—CPU, 50 GB RAM—of which eight parallel threads were used. The Elastix is programmed in C++, while the TM registration algorithm, utilizing the computations via spectral domain, was implemented in the MATLAB environment.

Results

Both registration methods were tested on the dataset containing 74 subjects. The whole data set was tested using ICE; out of them, 17 randomly chosen subjects were

		Frontal lo	Frontal lobe		Parietal lobe		CSF edge	
		TM	Elastix	ТМ	Elastix	TM	Elastix	
Aver	age mean	1.224	1.398	1.127	1.205	1.354	1.973	
Avera	age STD	0.096	0.156	0.114	0.146	0.206	0.602	

Table 6Average mean andSTD values marked edgecontinuity

	Occipital lobe		Temporal lobe		Midbrain	
	ТМ	Elastix	TM	Elastix	TM	Elastix
Average mean	1.088	1.164	1.114	1.248	1.161	1.915
Average STD	0.117	0.145	0.122	0.355	0.213	0.712

evaluated also by the two other criteria. Selected regions (frontal lobe, parietal lobe, temporal lobe, CSF, occipital lobe, and midbrain) were evaluated by the checkerboard method and the first four regions also by the NFI method. The suggested TM registration method worked reasonably for all subjects, while the reference method (Elastix) failed completely for three subjects (ICE~8.0). The results based on individual comparison criteria are in detail described below.

Evaluation by Inverse Consistency Error

Three basic statistical parameters from the ICE test were computed for all 74 subjects (Table 4). All the determined parameters proved to be better for the TM algorithm. The most significant parameter of registration quality is considered to be the mean ICE value [22].

Regarding the similarity criteria, the tested registration methods are different. However, the statistical results of two-sided Wilcoxon rank sum test and two sample t tests on the mean ICE values with 0.05 alpha level proved that template matching algorithm together with normalized cross-correlation criterion is a reliable method for the registration of FA and T1 images. This can be explained by the already mentioned positively monotonous dependence of the intensities between both FA and T1 modalities. Evaluation by the Checkerboard Classification Method

The average and standard deviation values representing the visual evaluation of the edge continuities within the checkerboard image are described in Tables 5 and 6. The differences between both evaluated registration methods are significant mainly in CSF and midbrain regions, while in the remaining regions, the registration quality can be considered comparable.

Three examples based on the checkerboard method are in Figs. 6, 7, and 8.

Evaluation by Nerve Fiber Intersection

Significant differences in the reliability of both tested registration algorithms were observed in the regions splenium of corpus callosum and genu of corpus callosum, when evaluated by the NFI criterion. These regions are considered the main parts of WM and thus critical places for brain connectivity determination [32]. The Elastix method was not fully accurate more frequently (in about 67 %) than TM (only about 40 %) in these regions. In addition, in the frontal lobe region, especially in its upper part, the TM registration has shown higher reliability (47 % failure versus 87 %). The TM registration and the Elastix method have led to slight misalignments in some of the peripheral parts of the frontal lobe and parietal lobe. Both methods have shown comparable



Fig. 6 Example of edge continuity showed by checkerboard technique (*left* affine registration, *middle* affine and elastix registration, *right* affine and template matching registration) **Fig. 7** Example of edge continuity showed by checkerboard technique (*left* affine registration, *middle* affine and elastix registration, *right* affine and template matching registration)



registering efficiency in the remaining regions of WM as seen in Figs. 9, 10, and 11.

Higher values of NFI (averages±standard deviations) inside the WM regions (Table 7) indicate slightly better fit of nerve fibers provided by the TM registration (Fig. 11), in some cases rather significant.

Precise evaluation of registration accuracy and robustness is

generally difficult for multimodal images, and when done

manually, it is dependent on previous evaluator's knowledge

and experience. According to publications mentioned in the

introduction [6, 16, 17], the FA and T1 images were so far

registered using either the ITK library or the Elastix.

However, the authors did not evaluate quantitatively either the accuracy or the robustness of the spatial alignment. We apply a methodology for a more quantitative evaluation by both automatic and visual criteria. The checkerboard method provides a good subjective overview of misalignments within the whole image by evaluation of edge discontinuities. The numerical and visual evaluation of the NFI criterion has proved to be a valuable method to evaluate the relative presence of nerve fibers inside the white matter, showing the degree of alignment. The ICE criterion, based on forward and backward determination of the displacement field, evaluates the robustness of the registration algorithms even more qualitatively.

The TM algorithm has shown a better robustness and reliability at the border of CSF region and surrounding tissues and inside the frontal lobe and midbrain regions.

eriginal elastix template matching



Discussion



Fig. 9 Example of NFI visual evaluation (*left* affine registration, *middle* affine and elastix registration, *right* affine and template matching registration)

The registration calculated by the Elastix based on B-splines provides slightly better match in some peripheral parts of frontal and parietal lobes. The NFI criterion was confirmed by the checkerboard method. Significant differences between both registration methods were found at the edge of the CSF region. Since this region represents very important area for brain connectivity detection, precise registration is essential here. Implementation Aspects

The computation time necessary to determine the final displacement field was approximately 80 s per subject for both methods. However, the TM algorithm offers still a great possibility of a further acceleration by more massive parallelization. Theoretically, the number of threads can be equal to the number of defined nodes in the image. Thus, there is



Fig. 10 Example of NFI visual evaluation (*left* affine registration, *middle* affine and elastix registration, *right* affine and template matching registration)



Fig. 11 Example of NFI visual evaluation (*left* affine registration, *middle* affine and elastix registration, *right* affine and template matching registration)

still a potential for a substantial further speed-up, particularly when implemented on a GPU [33]. The last version of the parallel MATLAB toolbox (2011a) supports up to 16 simultaneously working labs, thus potentially offering the reduction in computation time by the factor of two. Elastix utilizes parallelization in principle as well. However, the tested configuration did not support the present parallel processing, when using the parameters according to the Table 3.

The TM algorithm, in general, can use any similarity criterion, but in order to keep the computation time as low as possible, the criteria convertible to the Fourier space are preferable. This leads to the use of correlation based criteria; among them, the correlation coefficient is insensitive to linear contrast transforms and has proved, in experiments, robust even to nonlinear monotonous non-decreasing intensity dependencies [21].

Although the proposed registration method provided very good spatial alignment of FA and T1 images, further development may still be considered. So far, the TM algorithm is based on user-defined equidistant grid spacing and also mask and searched neighborhood sizes; this rigid setting can be suboptimal in some cases. The grid of nodes carrying displacements, which is thus regular so far, may be changed

Table 7 Statistics ofNFI values inside the		TM	Elastix
WM region	Average	0.285	0.221
	STD	0.022	0.019

to an adaptive one with spatially uneven distribution; this might improve the computational speed as well as the quality of detailed registration. The displacement field can also be calculated using a multilevel (pyramidal) approach, where both the neighborhoods and masks are ever smaller on a next level; this could further improve the reliability of registration. Further, spatially variable adaptive form of Gaussian filtering of the derived displacement field could improve the accuracy, particularly in peripheral brain regions. In addition, detection of rotation based on a cylindrical phase correlation method [34] might lead to improving the quality in peripheral brain regions. These modifications that would possibly result in both higher reliability of local displacements and better details in the displacement field will be the subject of further research.

Conclusion

In this paper, we have proposed an intrasubject registration method of MR fractional anisotropy images (FA) and T1weighted anatomy images (T1) of healthy human brain. The registration procedure using TM registration based on the normalized cross-correlation similarity criterion was compared with the multimodal NMI-based registration provided by the Elastix software, considered the reference method. The nonlinear dependency of intensities between FA and T1 images was confirmed, and consequently, the normalized cross-correlation criterion was successfully implemented in the TM algorithm, calculated via the spectral domain. According to the presented results, the TM algorithm provided better local alignment and registration stability than mutual information in Elastix. Therefore, the TM method can be considered as a suitable, fast, and robust approach to registration of FA images with corresponding T1 images. Although the peripheral brain regions are very complicated, the chosen configuration of the TM algorithm provided more reliable results in all our experiments.

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